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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/457,771	12/09/1999	R. MARTIN EMANUELE	19720-0624	8054

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/457,771	EMANUELE ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-4,6,7,9-12,14,15 and 17-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-4,6,7,9-12,14,15 and 17-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 July 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/15/04 has been entered.

Claims 8 and 16 were canceled and new claims 32-34 were added as requested.

Claims 1-4, 6, 7, 9-12, 14, 15, and 17-34 are pending and under consideration in this Office Action.

On 7/28/2000, Applicant filed a request for a continuing prosecution application, including a new specification, and copies of the original claims, abstract, drawings and oaths. These documents were made of record and replace the original specification, claims, drawings, abstract, and oaths.

Rejections Withdrawn

The rejections of claims 17, 20, 27, and 31 under 35 USC 112, second paragraph are withdrawn in view of Applicant's amendments.The rejection of claims 1, 8, 17, 18, and 24-28 under 35 U.S.C. 102(e) as being anticipated by Lee is withdrawn in view of Applicants amendments requiring that the polyoxyethylene (POE) portion of the copolymer must less than 45% of the total weight of the copolymer. The rejection of

claims 25, 28, and 30 under 35 USC 103 over Torrence and Lee is withdrawn in view of Applicants amendments requiring that the polyoxyethylene (POE) portion of the copolymer must less than 45% of the total weight of the copolymer.

Drawings

The drawings filed 12/9/99 were objected to by the Draftsman for the reasons set forth in the PTO Form 948 attached to Paper No. 24 mailed 10/10/03. New drawings were received on 7/28/2000, but these drawing appeared to be identical to those originally filed, so the objection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6-12, 14-31, and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4, 6-12, 14-31, and 34 are indefinite because the intended scope of the nucleic acids intended to be embraced is unclear. Specifically, it is unclear if Applicant intends to claim compositions comprising oligonucleotides such antisense , triplex formers, and ribozymes, or whether Applicant intends to claim expression vectors encoding such oligonucleotides.

Response to Arguments

Applicant's arguments filed 4/15/04 have been fully considered but they are not persuasive. Applicant argues that the claims as amended are definite. This is unpersuasive. The claims read: "expression vectors which encode gene products, genes, oligonucleotides, antisense oligonucleotides, triplex DNA compounds, ribozymes and mixtures thereof." It remains unclear as to whether or not Applicant intends the "genes, oligonucleotides, antisense oligonucleotides, triplex DNA compounds, ribozymes and mixtures thereof" to be encoded by the expression vector, or whether these items are independent nucleic acids not associated with any expression vector. This claim can be interpreted as being drawn to expression vectors that encode any of the species that follow in the claim, or as being drawn to expression vectors encoding gene products.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6, 7, 9, 14, 15, and 17-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 6, 7, 9, 14, 15, and 17-33 recite the limitation "the polyoxyethylene portion of the block copolymer is less than 45% of the total weight of the block copolymer". This phrase is interpreted as a range from 0% to 45%. The specification provides no written support for this particular range, so it represents new matter. The specification provides written support for 1% to 50%, and for 5% to 20%, but does not provide support for the range of 0-45%, and there is no evidence that Applicant contemplated this specific range at the time the invention was filed.

Claims 32 and 33 require that the hydrophobe portion must be between approximately 500 and 1000 Da. The specification provides no written support for this range, in fact the specification does not disclose any copolymer in which the hydrophobic portion is less than 750 Da. As such, there is no evidence that Applicant contemplated this specific range at the time the invention was filed, and it represents new matter.

Claim 33 requires that the polyoxyethylene portion of a block copolymer must be "approximately 10% -30% of the total weight of the block copolymer. The specification provides no written support for this range, and there is no evidence that Applicant contemplated this specific range at the time the invention was filed, so it represents new matter.

Claim 34 requires that the polyoxypropylene portion of a copolymer must be "between approximately 4400 and 15000 Daltons". The specification provides no written support for this range, and there is no evidence that Applicant contemplated this specific range at the time the invention was filed, so it represents new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 9-12, 17, 19, and 20 stand rejected under 35 U.S.C. 102(e) as being anticipated by Allison et al (US Patent 5,376,369, issued 12/27/94) as evidenced by .

Allison taught that Pluronics L101, L121, and L122, could be used as an adjuvant in the delivery of whole viruses in vivo as vaccines (see abstract, and column 23, lines 24-55, especially, lines 30, 31, 34, 36, 38, 46, and 55). Note that L101 and L122 are the trade names for CRL 8131 and CRL 8142, respectively (see e.g. Table II at page 17 of instant specification). Whole viruses comprise nucleic acids encoding genes, and can be considered expression vectors. The limitation requiring an expression vector capable of expressing the genes is anticipated by the viruses themselves, which are clearly capable of expressing their own genes. Because the viruses comprise genes required for viral transcription, they comprise genes that are used for altering gene activity, particularly during the process of viral amplification

Thus Allison anticipates the claims.

Claims 1-3, 9-11, 17, and 19-21 stand rejected under 35 U.S.C. 102(e) as being anticipated by Wasmoen et al (US Patent 5,656,275, issued 8/12/97), as evidenced by Osorio et al (WO 99/39733, issued 8/12/99).

Wasmoen taught that Pluronic L121 could be used as an adjuvant in the delivery of whole viruses in vivo (see column 3 line 66 to column 4, line 28). Whole viruses comprise nucleic acids encoding genes, and can be considered expression vectors. To the extent that the viruses must be propagated in order to make the disclosed vaccines, the nucleic acids are amplified. The limitation requiring an expression vector capable of expressing the genes is anticipated by the viruses themselves, which are clearly capable of expressing their own genes. The compositions can be considered to comprise an antimicrobial drug (claim 18) in the form of viral antigens. Because the viruses comprise genes required for viral transcription, they comprise genes that are used for altering gene activity, particularly during the process of viral amplification. The viruses are modified to express foreign antigens for the purpose of providing an immune response against the antigens. It is noted that Wasmoen exemplifies a virus in which the antigen is expressed and incorporated into the viral particle, prior to administration of the virus to a recipient animal. However, a review of the art indicates that the virus of Wasmoen should be capable of infecting cells in vivo and subsequently producing a foreign antigen in infected cells in vivo, thereby meeting the limitations of claims 21 and 29. See Osorio et al who teach recombinant raccoon poxviruses similar to those of Wasmoen, containing foreign genes encoding antigens and immunomodulatory factors for expression in the recipient (page 6, line 22 to page 7, line 10, page 7, line 21 to page 8, line 7, page 10, lines 4-22.

Thus Wasmoen anticipates the claims.

Response to Arguments

Applicant's arguments filed 4/15/04 have been fully considered but they are not persuasive.

Applicant argues at page 11 that Allison fails to anticipate the claims because the compositions and methods relied upon from the disclosure of Allison also comprise an immunopotentiating amount of a muramyldipeptide, a whole virus, and a glycopeptide. Applicant argues that the inventions are distinct because the instant invention does not require a muramyldipeptide, a whole virus, or a glycopeptide. This is unpersuasive because the instant claims do not exclude these agents. Applicant's assertion that Allison fails to teach all of the limitations of the claims is unpersuasive because Applicant fails to point out which limitation Allison fails to teach.

Regarding the rejection of Wasmoen as evidenced by Osorio, Applicant argues teachings of Wasmoen relied upon in the rejection are not enabled. For support Applicant relies Osorio, noting that Osorio teaches that an adjuvant is not essential for poxvirus vaccine production, and would in some cases preclude the advantages of a poxvirus vaccine. This argument is unpersuasive because Applicant has provided no evidence or reasoning to indicate that the use of L121 would render inoperative the invention of Wasmoen. Absent such evidence or reasoning, the invention is considered to be enabled. Applicant argues further that in the invention of Wasmoen it is not the viral nucleic acid per se that is required for vaccine activity, but rather the protein antigens in the virus particle. This is unpersuasive because, as noted in the rejection, a review of the art indicates that the virus of Wasmoen should be capable of infecting

cells in vivo and subsequently producing a foreign antigen in infected cells in vivo, thereby meeting the limitations of claims 21 and 29. See Osorio et al who teach recombinant raccoon poxviruses similar to those of Wasmoen, containing foreign genes encoding antigens and immunomodulatory factors **for expression in the recipient** (page 6, line 22 to page 7, line 10, page 7, line 21 to page 8, line 7, page 10, lines 4-22. Finally Applicant argues that Wasmoen and Osorio fail to teach the addition of a low molecular weight alcohol or Tween 80. This is unpersuasive because the rejected claims do not recite low molecular weight alcohol or Tween 80 as limitations. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, 7, 9, 14, 15, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wasmoen et al (US Patent 5,656,275, issued 8/12/97) in view of Miyamura et al (US Patent 5,372,928, issued 12/13/94).

Wasmoen taught that Pluronic L121 could be used as an adjuvant in the delivery of whole virus vaccines in vivo (see column 3 line 66 to column 4, line 28). Whole

viruses comprise nucleic acids encoding genes, and can be considered expression vectors. To the extent that the viruses must be propagated in order to make the disclosed vaccines, the nucleic acids are amplified. Note that L121 has a hydrophobe molecular weight of about 4400, which is within 10% of the recited "approximately 4400", and so is considered to be within the claimed range. The hydrophile percentage of L121 is about 90%.

Wasmoen did not teach the addition a surfactant and an alcohol to the vaccine.

Miyamura teaches that vaccine compositions are often modified by the addition of ethanol and Tween 80. See e.g. column 19, lines 5-22. Arriving at the appropriate concentrations of these additives is considered to be routine optimization.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 4/15/04 have been fully considered but they are not persuasive.

Applicant argues at page 14 of the response that Miyamura fails to teach the or suggest the combination of ethanol and Tween 80 as claimed, noting that the reference requires three bacterial components in conjunction with Tween 80 and squalene to be effective. This argument is unpersuasive because Miyamura clearly states that ethanol is a useful vaccine excipient, and that the vaccine may further comprise the requires three bacterial components, Tween 80, and squalene. See column 19,lines 5-22. As adjuvant components, the concentrations of Tween 80 and ethanol are considered to be

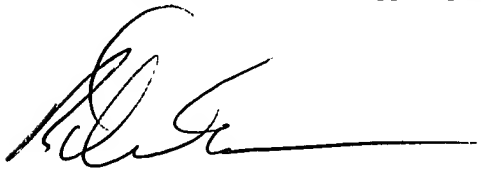
result-effective variables, and as noted above, arrival at the optimum concentrations of ethanol and Tween 80 is considered to be to be routine optimization of such variables. See MPEP 2144.05 (II).

Conclusion

No claim is allowed. Claims 18 and 22-32 are free of the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.



Richard Schnizer, Ph.D.